# Extended Release Tablets Containing High Levels of Carbomer Homopolymer

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## OBJECTIVE

To identify the feasibility of incorporating high levels (up to 20% w/w) of Carbopol® 971P NF polymer (Carbomer Homopolymer Type A) as an extended release matrix former in tablets.

## METHODOLOGY

### Materials

Guaifenesin (Delta Synthetic Co. Ltd., Taiwan), Carbopol® 971P NF polymer (Lubrizol Advanced Materials, Inc., Cleveland, OH), Emcocel® 50M microcrystalline cellulose (JRS Pharma LP, Patterson, NY), Lactose monohydrate (Sheffield Pharma Ingredients, Norwich, NY), Synpro® magnesium stearate (Ferro Corporation, Walton Hills, OH) Ketoprofen (Medisca Inc., Plattsburgh, NY), Talc (Acros Organics USA, Morris Plains, NJ), Cab-O-Sil® M5 fumed silica (Cabot Corporation, Billerica, MA)

### Methods

Several formulations containing guaifenesin or ketoprofen as model water soluble and low water soluble drugs, respectively, and polymer levels ranging from 5 to 20% w/w were prepared (Table 1). The formulations were wet granulated with a rate-controlled addition of deionized water in a high shear granulator (Glatt, E-150). The wet granules were tray-dried, sized and after magnesium stearate addition, compressed into tablets on a rotary tablet press (Korsch, PH-103).

The granules were evaluated for flow rate, critical orifice diameter, bulk and tapped densities and Carr's compressibility index. The tablets were evaluated for weight variation, hardness, friability and dissolution properties.

**Table 1. Composition of tablet formulations**

| | Composition (% w/w) | | | | | |
|---|---|---|---|---|---|---|
| | Guaifenesin | | | Ketoprofen | | |
| Ingredients | G1 | G2 | G3 | K1 | K2 | K3 |
| Guaifenesin | 75 | 75 | 75 | | | |
| Ketoprofen | | | | 66.67 | 66.67 | 66.67 |
| Carbopol® 971P NF polymer | 5.0 | 10.0 | 20.0 | 10.0 | 15.0 | 20.0 |
| Emcocel® 50M microcrystalline cellulose | 5.0 | 5.0 | 4.5 | 7.12 | 5.44 | 3.78 |
| Lactose monohydrate | 14.5 | 9.5 | | 14.22 | 10.89 | 7.56 |
| Talc | | | | 0.5 | 0.5 | 0.5 |
| Cab-O-Sil® M5 fumed silica | | | | 0.5 | 0.5 | 0.5 |
| Magnesium stearate | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| **Total** | **100.0** | **100.0** | **100.0** | **100.0** | **100.0** | **100.0** |

## RESULTS

20% w/w Carbopol® 971P NF polymer could be incorporated in the guafenesin formulations with a low water amount (5% w/w) and low spray rate (1.29% w/w/min) (Table 2). The processing conditions optimized for incorporating 20% w/w polymer could be extrapolated to formulations containing lower levels of polymer inclusion (5% w/w). The formulations developed showed acceptable granule and tablet properties (Tables 3 and 4). The release of guaifenesin in different media was found to be inversely proportional to the incorporated polymer level (Figures 1 and 2). It was also observed that increasing polymer levels resulted in a more robust formulation i.e. a reduction in intra-batch variability, particularly in 0.1N HCl (Figure 2).

**Table 2. Processing conditions for high shear granulation**

| Process | Formulations | |
|---|---|---|
| | Guaifenesin | Ketoprofen |
| **Dry mixing** | | |
| Speed (impeller / chopper) rpm | 300/500 | 300/500 |
| Mixing time (min.) | 6 | 6 |
| **Spraying** | | |
| Speed (impeller / chopper) rpm | 400/750 | 400/750 |
| Spray rate (% w/w/min) | 1.29 | 3.66 |
| **Wet massing** | | |
| Speed (impeller / chopper) rpm | 600/300 | 600/300 |
| Time (min) | 1.0 | 1.0 |
| **Total water added (% w/w)** | 5 | 17.5 |

**Table 3. Physical properties of guaifenesin formulation granules**

| Batch (% w/w Carbopol® 971P NF polymer) | Flodex (mm) | Flow rate (g/sec) | Bulk density (g/cc) | Tapped density (g/cc) | Carr's compressibility index (%) |
|---|---|---|---|---|---|
| G1 (5%) | 8 | 6.71 | 0.385 | 0.506 | 23.92 |
| G2 (10%) | 7 | 6.32 | 0.370 | 0.447 | 17.24 |
| G3 (20%) | 6 | 6.80 | 0.393 | 0.500 | 21.33 |

**Table 4. Physical properties of guaifenesin tablets**

| Batch (% w/w Carbopol® 971P NF polymer) | Weight (mg) | | Thickness (mm) | | Hardness (kp) | | Friability 100 rot. | Friability 300 rot. |
|---|---|---|---|---|---|---|---|---|
| | mean | SD | mean | SD | mean | SD | | |
| G1 (5%) | 800.74 | 4.48 | 7.19 | 0.01 | 16.09 | 0.51 | 0.17 | 0.25 |
| G2 (10%) | 800.09 | 3.61 | 7.21 | 0.02 | 20.15 | 0.63 | 0.18 | 0.21 |
| G3 (20%) | 799.38 | 4.21 | 7.67 | 0.02 | 14.03 | 0.70 | 0.28 | 0.49 |

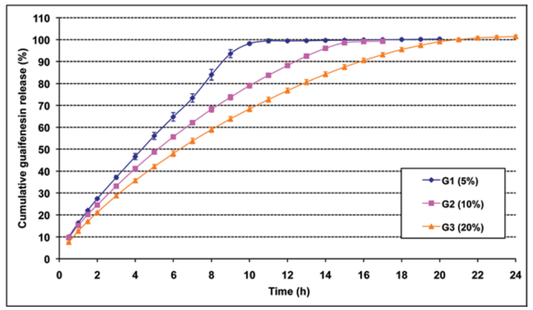


*Figure 1. Influence of Carbopol® 971P NF polymer level on the release of guaifenesin in pH = 6.8 phosphate buffer*

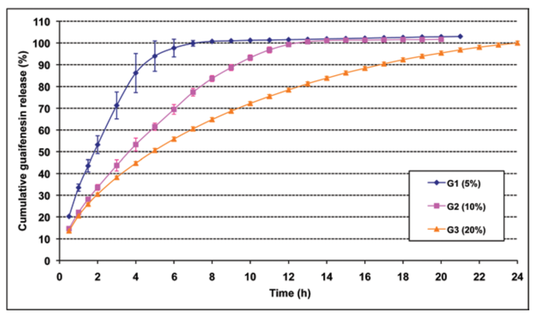


*Figure 2. Influence of Carbopol® 971P NF polymer level on the release of guaifenesin in 0.1N HCl*

For ketoprofen formulations, incorporating higher polymer levels (20% w/w) required lower drug loading (66.67% w/w) and an increase in the rate (3.66% w/w/min) and amount (17.5% w/w) of granulating water (Table 2). The formulations developed showed acceptable granule and tablet properties (Tables 5 and 6). Since the amount of granulating water added depended on the polymer level and is critical to the reproducibility of a formulation, the conditions optimized for incorporating 20% w/w polymer could not be easily extrapolated to formulations containing polymer levels below 15% w/w. At lower polymer levels, the formulations required significantly higher levels (up to 30% w/w) of granulating water. Increasing polymer levels slightly decreased the release of ketoprofen in phosphate buffer pH = 6.8 (Figure 3).

**Table 5. Physical properties of ketoprofen formulation granules**

| Batch (% w/w Carbopol® 971P NF polymer) | Flodex (mm) | Flow rate (g/sec) | Bulk density (g/cc) | Tapped density (g/cc) | Carr's compressibility index (%) |
|---|---|---|---|---|---|
| K1 (10%) | 10 | 3.81 | 0.385 | 0.488 | 21.08 |
| K2 (15%) | 6 | 4.66 | 0.395 | 0.482 | 18.07 |
| K3 (20%) | 6 | 5.35 | 0.405 | 0.506 | 19.99 |

**Table 6. Physical properties of ketoprofen tablets**

| Batch (% w/w Carbopol® 971P NF polymer) | Weight (mg) | | Thickness (mm) | | Hardness (kp) | | Friability 100 rot. | Friability 300 rot. |
|---|---|---|---|---|---|---|---|---|
| | mean | SD | mean | SD | mean | SD | | |
| K1 (10%) | 299.68 | 5.10 | 4.97 | 0.02 | 10.01 | 0.94 | 0.23 | 0.64 |
| K2 (15%) | 299.08 | 3.82 | 4.99 | 0.02 | 10.26 | 1.29 | 0.19 | 0.51 |
| K3 (20%) | 300.71 | 3.25 | 4.99 | 0.02 | 9.93 | 0.72 | 0.20 | 0.53 |

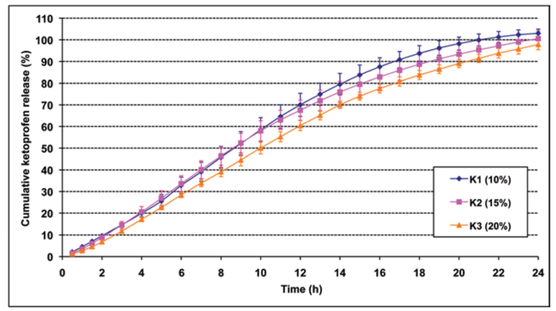


*Figure 3. Influence of Carbopol® 971P NF polymer level on the release of ketoprofen in pH = 6.8 phosphate buffer*

## CONCLUSIONS

- 20% w/w Carbopol® 971P NF polymer was successfully incorporated into extended-release tablet formulations containing a water-soluble (guaifenesin) and a low water soluble (ketoprofen) drug.
- Incorporating 20% w/w polymer in formulations containing a water-soluble drug was achieved with a low water level (5% w/w) and a low water spray rate (1.29% w/w/min); whereas in formulations containing a low water soluble drug, incorporating 20% w/w polymer required higher water levels (17.5% w/w) at a higher spray-rate (3.66% w/w/min).
- For guaifenesin formulations, increasing the polymer level from 5 to 20% w/w resulted in a progressive retardation of drug release with a reduction in intra-batch variability. These effects were found to be consistently reproducible in pH = 6.8 phosphate buffer and 0.1N HCl.
- For ketoprofen formulations, increasing polymer levels from 10 to 20% w/w slowed the drug release with a reduction in intra-batch variability. Inclusion of 20% w/w polymer resulted in a robust formulation. The low solubility API required stricter control of the granulating conditions, thus making it more difficult to extrapolate to lower polymer levels (require higher amount of water).

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